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Implantable electrochemical redundant micro-sensor arrays for glucose monitoring patterned polymer films

### Introduction

Development of a highly miniaturized, redundant multianalyte microsensor arrays to monitor metabolites either in blood stream or in soft tissue is essential. Such a sensor arrays, we anticipate will monitor multiple analytes simultaneously. Introduction of redundancy in the sensor will enable measurements to be derived from the average of the signal resulting from each array element. Previously described technology will be used to fabricate redundant multianalyte microsensor arrays for glucose, lactate, and pyruvate. In this first part we have focused on sensing glucose especially important in diabetic patients. Diabetes is already a modern epidemic. More than five percent of North Americans have diabetes—high blood sugar levels —and this number is expected to double by 2010. Some reports suggest that this percentage of North Americans with diabetes may be 50 percent higher. It is the leading cause of blindness and kidney failure among others. Intensive treatment with the goal of maintaining blood glucose concentrations close to the normal range can prevent or delay the occurrence of diabetic related complications. The diabetics therefore have to frequently monitor their glucose levels by pricking their fingertips to draw blood necessary for conventional glucose monitoring. The blood data obtained with these meters does not indicate the direction or trend of blood sugar levels. Even the most motivated diabetic patient performing frequent tests may miss reoccurring highs or lows, particularly at night.

Glucose sensors that use enzyme (glucose oxidase) to achieve specificity are currently not stable or sensitive enough to meet the demands of a closed loop delivery system. As a result, over the counter glucose meters are used to closely monitor the glucose levels in the body. Frequent skin punctures to obtain blood samples several times a day is painful, aesthetically unpleasant and inconvenient approach. This work is aimed at developing highly miniaturized, implantable, micro-array sensor for real-time continuous glucose monitoring. These sensor arrays are micro-fabricated on flexible plastic substrates. Development of an implantable glucose monitoring technique will resort in increased patient compliance with intensive glucose management regimes and will help decrease the frequency of hypoglycemic episodes because of the increased awareness of blood glucose levels.

## **Body**

#### Background

A number of strategies for measuring the blood glucose are continuously under development to allow pain free, more frequent glucose monitoring. Transdermal spectroscopic<sup>2,3</sup> and interstitial fluid sampling<sup>4,5</sup> are some of the techniques under investigation. The transdermal spectroscopic techniques are painless a major advantage. However, their main drawback is measurement of glucose in a highly complex matrix of water, proteins polysaccharides and lipids. The result is a complex signal with glucose measurement having to be extracted through other mathematical programs hence introducing errors at every stage. Reverse iontophoresis <sup>6</sup> and sonophoresis <sup>7</sup> techniques for interstitial blood sampling have been studied. One advantage of these techniques is that a physiologically relevant fluid sample with glucose concentration closely

related to glucose in blood is collected. There still exists significant difference between the blood plasma glucose and interstitial fluid glucose.<sup>8</sup>

Implantable sensors for glucose have been under investigation for nearly three decades with mixed and promising results. Implantation of sensors can be done either in subcutaneous tissue to measure glucose in interstitial fluid<sup>9,10,11,12</sup> or intravascular.<sup>13</sup> These sensors have enormous potential for long term monitoring of glucose in humans as demonstrated from limited clinical trials. As with any foreign object introduced into the body, biocompatibility is one of the most important requirements of these sensors. Additionally, in the case of blood-contacting devices, the hemocompatibility of in vivo sensors is an important consideration, as well. Adsorption of proteins on surfaces of implanted sensors and devices constitutes the first step of several biological responses, including the activation of the coagulation cascade. Following protein adsorption, cell adhesion occurs. This is generally an undesirable event, since it could lead not only to the alteration of the sensor output but also to harmful side effects on the subject, e.g., thrombi formation after adsorption and activation of platelets.<sup>14</sup> In this work hydrogel networks will provide an ideal three-dimensional, aqueous in vivo-like surrounding.<sup>15, 16, 17, 18</sup>

Most glucose monitors based on biosensor technology currently operate on principle that glucose reacting with a glucose-specific enzyme produces hydrogen peroxide that can be detected electrochemically. The hydrogen peroxide produced is detected on a platinum electrode. Two electrons are measured on the electrode as an electric current by an external circuit. This sensing scheme has some limitations. The glucose concentration in blood is higher than the  $O_2$  concentration. Membranes are thus required to slow glucose transport in order to prevent an  $O_2$ -limited reaction. Also, at the electrode potential necessary for detecting hydrogen peroxide, other blood components such as ascorbic acid can interfere with the measurement. To eliminate this problem redox polymers exchange electrons with glucose oxidase at near zero potential can be used.  $^{19,20}$ 

A high degree of miniaturization is crucial to make the introduction of the sensor as minimally invasive as possible and relieve any unnecessary burden on the patient. The integration of the sensor into an existing implanted device (such as a pressure catheter) is highly desirable. As we had proposed, we have taken advantage of silicon micro fabrication technologies to develop implantable micro-sensor arrays of biorecognition molecules immobilized in photopolymerized and microlithographically patterned polymer films. We have focused on glucose oxidase immobilized in redox polymer hydrogels. Redox polymers are polymers that contain electron acceptor/donor groups. Amperometric biosensors based on redox polymer/enzyme complexes were shown to be miniaturizable and implantable. 21,22,23 In this work redox polymers exchange electrons with glucose oxidase entrapped in biocompatible poly-ethylene glycol diacrylate (PEG-DA) macromolecular networks. The PEG-DA hydrogel acted to cross-link the redox polymer and glucose oxidase. Cross-linking occurs by reaction of pyridine nitrogen's and amine functions of the enzyme, as well as redox polymer with PEG.<sup>24</sup> Other electrostatic interactions also help stabilize the sensor. The entrapped glucose oxidase through cross-linking was found to oxidize glucose in buffer solution as will be demonstrated later. In this research group, enzymes entrapped in redox hydrogels using photopolymerization have been shown to retain their activity. 25,26,27,28,29 The two approaches to enzyme entrapment will be explored.

Synthesis of poly[vinylpyridine Os(bis-bipyridine)<sub>2</sub>Cl] (redox polymer)

Synthesis of poly[vinylpyridine Os(bis-bipyridine)<sub>2</sub>Cl], an osmium based polycationic redox polymer was done following modifications of established protocols<sup>30</sup>. Os(bpy)<sub>2</sub>Cl<sub>2</sub> was synthesized according to a standard procedure with minor modifications.<sup>31</sup> In brief two equivalents of bipyridine (1440mg) were mixed with one equivalents ammonium hexachloroosmate (IV) (2000mg) in 100mL ethylene glycol. The mixture was heated to reflux for 45 minutes and then precipitated with supersaturated sodium diothionate. The precipitate was repeatedly washed with water and finally with ether. The Os(bpy)<sub>2</sub>Cl<sub>2</sub> was used for synthesis of photocrosslinkable redox polymers in these studies.

Os(bpy)<sub>2</sub>Cl<sub>2</sub> (0.988 g, 1.728 mmol) and poly(4-vinyl-pyridine) (0.860 g, 8.18 mequiv) were heated under nitrogen at reflux in 36 mL of ethylene glycol for 2 hours. The solution was then cooled down to room temperature and 60 mL of DMF and 3.0 g of 2-bromoethylamine hydrobromide (14.6 mmol) were added and then stirred overnight at 45 °C. A crude polymer precipitate was formed by pouring the solution into rapidly stirred acetone. The hygroscopic precipitate was collected and dissolved in H<sub>2</sub>O. The solution was filtered and precipitated as the PF<sub>6</sub> salt by addition of a solution of NH<sub>4</sub>PF<sub>6</sub>. The precipitate was dried in a vacuum at 40°C. 0.98g of the dry PF<sub>6</sub> salt was dissolved in 40 mL of acetonitrile and then diluted with 100 mL of H<sub>2</sub>O and stirred over 10.4 g of anion exchange beads for 2 hours. The solution was filtered and evaporated under vacuum to ~20mL. Concentrated HCl was added to the solution to adjust to pH 2. The solution was then dripped into rapidly stirred acetonitrile. A precipitate that formed was filtered and dried in a vacuum desiccator. The pure product was analyzed.

Figure 1. Structure of poly[vinylpyridine Os(bis-bipyridine)<sub>2</sub>Cl] (POs-Ea) molecule containing osmium redox polymer backbone.

## Fabrication of electrode arrays

Mylar and Polyimide sheets were purchased from Mcmaster-carr and washed with ethanol. These are flexible insulating materials and ideal platforms for electrode manufacturing. Square pieces of both mylar and polyimide were cut before coating with positive photoresist (MAP-100). Modified literature procedure was used to fabricate the electrode arrays. In brief positive photoresist (Map-100) was deposited on square polymer sheets and spin coated at 4000 rpm for 30 seconds and then soft backed at 100°C for 6 minutes. These polymer sheets with dry photoresist were brought in close contact with the photo-mask and exposed to 365nm, 450mJ/cm<sup>2</sup>. The polymer sheets were then placed in developer solution (Ma-D 330) for seventy seconds to remove

portions of photoresist that were exposed to UV light. The sheets were then rinsed with distilled water.

To make different thicknesses of the patterns, MAP-100 photoresist was spin coated on the polymer sheets at 300rpm for 2 minutes and then baked at 100°C for one hour and twenty minutes. The thickness of the film made was estimated at 30µm. Exposure to UV was done at 365nm, 2200mJ/cm<sup>2</sup>. The sheets were placed in the developer solution for ten minutes.

The photoresist patterns were then sputter coated with  $100~\text{A}^{\circ}$  adhesion layer of chrome followed by  $1500~\text{A}^{\circ}$  layer of gold (done at Pennsylvania state university using Lesker CMS-18 sputtering tool and by Lance Goddard Associates at Foster City, CA). The photoresist was removed using ethanol lifting-off chrome and gold from all non-patterned areas. The result was distinct patterns of gold with  $500\mu m$  diameter electrodes with leads  $10\mu m$  and contact pads at 2.5mm x 2.5mm. Wires were attached to the contact pads by using conductive silver epoxy resin (Ladds Research, Williston, VT).

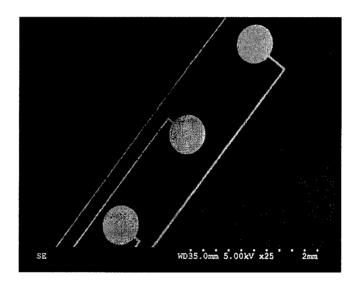


Figure 2 Electrode redundant array fabricated on both flexible mylar and polyimide sheets showing transmission microscopy image

# Film deposition

The electrode arrays were functionalized with a carboxylic end group by immersing in 2mM MUA in ethanol for 20 minutes and then washed with ethanol. The electrodes were then dried under nitrogen. The thiol end group was chemisobed to gold to provide an anchor. Sequential deposition of redox polymer (POs-Ea, 5mg/ml), glucose oxidase (2mg/ml) in HEPES buffer, and PEG-DA (2mg/ml) was done on the functionalized electrodes. These solutions were mixed and left overnight at room temperature to cure. The modified electrodes were washed with water to remove any molecules not cross-linked at the surface of the electrode.

#### Electrochemistry

Electrochemistry was performed using Princeton applied research (PAR) 273 potentiostat. A three electrode system was used with platinum wire as counter electrode and Ag/AgCl as reference electrode. The array electrodes with enzyme, redox polymer and PEG-DA were used as working electrodes. All electrochemistry was done in 20mM PBS buffer pH 7.0.

# **Key research accomplishments**

- Successively synthesized an osmium based polycationic redox polymer (POs-Ea) a molecule that is responsible for exchanging electrons with glucose oxidase enzyme.
- Used photolithography to fabricate patterned sensor arrays on flexible plastic substrates (mylar and polyimide).
- Successively crosslinked active glucose oxidase enzyme with redox polymer and biocompatible polyethylene glycol diacrylate hydrogel.
- Used amperometry and cyclic voltammetry to confirm activity of the enzyme and contribution of each sensor array element.
- The enzyme exchanged electrons with redox polymer both entrapped in a hydrogel network

# Reportable outcomes

Each sensor array element was smooth and without any discontinuities. To determine whether the array elements had any connectivity problems, or whether they functioned independently cyclic voltammetry was done on each array member. Votammetry experiments were done initially without the substrate to evaluate the stability of the film. The formal potential of this redox polymer was around 0.3 V versus Ag/AgCl electrode about the same as what has been reported for this molecule.<sup>32</sup> Anodic and cathodic peaks were observed at 0.32 and 0.26mV versus Ag/AgCl reference electrode at 20mV/s scan rate. The peak separation was approximately 60mV. Figure 3 shows cyclic voltammograms of one element of micro-array at different scan rates. Plots of peak current versus scan rate were linear at scan rates 0.01-0.50 V s<sup>-1</sup>. At high scan rates (above 50mV/s) a deviation from linearity was observed (not shown). A plot of peak current (i<sub>p</sub>) versus square root of scan rate (v<sup>1/2</sup>) yielded a straight line (Figure 4). The dependence of the current function i<sub>p</sub> on the scan rate , v<sup>1/2</sup> is an important diagnostic criterion for establishing the type of mechanism by cyclic voltammetry.<sup>33</sup> The ratio of anodic to cathodic peak currents was unity indicating chemical reversibility. The CV are consistent with non-ideal, reversible, thin layer electrochemistry.<sup>34</sup>

Each electrode  $500\mu m$  in diameter was individually addressable. The micro-fabrication process was quite reproducible as observed from almost overlaid cyclic voltammograms for each member. The cross-linking of the redox polymer, glucose oxidase and PEG-DA is uniform on all the electrodes a very important result especially when the arrays sensors signals are to be summed up. The signal from all the array sensor elements mimics the behavior of one large sensor with electrode area equal to the sum of all the electrode array elements.

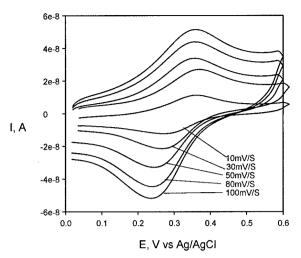


Figure 3. Cyclic voltammograms from one member of micro-array

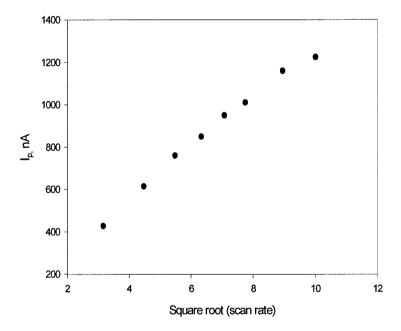


Figure 4. Scan rate dependence of film containing GOX, redox polymer and PEG-DA in phosphate buffer

Figure 5 shows cyclic voltammograms of increasing number of array elements. Measurements done after a combination of array members show corresponding increase in peak currents, a significant result that will make it possible to estimate the number of array members that are combined. It also suggests no cross-talk problems between the array members.

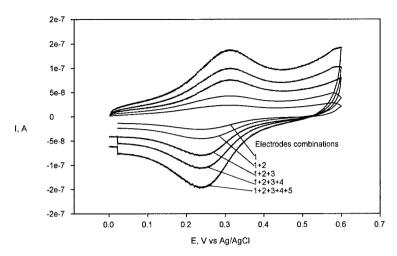


Figure 5. Cyclic voltammograms of different combinations of micro-array electrodes at 20mV/s scan rate

Biocompatible PEG-DA was used to cross-link glucose oxidase enzyme and electroactive redox polymer POs-Ea. Properly cross linked molecules are expected to retain the activity of glucose oxidase enzyme. Figure 6 shows cyclic voltammogram of one element of the micro-array in buffer and in buffer containing 10mM glucose solution. In presence of glucose the redox polymer reduction peak disappears and the oxidation peak current is enhanced. Flavin adenine dinucleotide of glucose oxidase GOX(FAD) reacts with β-D-glucose to form a reduced form GOX(FADH<sub>2</sub>) and gluconic acid and hydrogen peroxide. The reduced form of GOX (FADH<sub>2</sub>) is intern oxidized by the electrochemically generated Os<sup>2+</sup> form of the redox polymer, setting up a catalytic pathway which produces an enhanced oxidation peak. The electrons are transferred from the enzyme to the redox polymer, shuttled between the redox sites in self exchange reaction until being transferred to an electrode surface. The catalytic current produced is proportional to the glucose concentration. Presence of oxygen does not influence the rate of the reaction and hence the catalytic current obtained. Figure 7 shows the schematic chemical reactions that occur in this sensor.

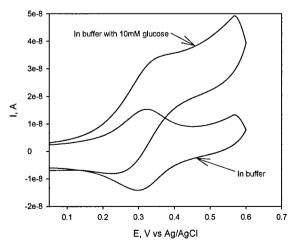


Figure 6 Cyclic Voltammograms showing activity of glucose oxidase in buffer and in buffer containing 10mM glucose at 20mV/s scan rate

Glucose oxidase is securely trapped in the polycationic redox polymer and hydrogel network and glucose diffuses through to access the glucose oxidase sites. Cross-linking occurred by reaction of pyridine nitrogen's and amine functions of the enzyme, as well as POs-Ea with PEG-DA. Other electrostatic interactions also help stabilize the film.

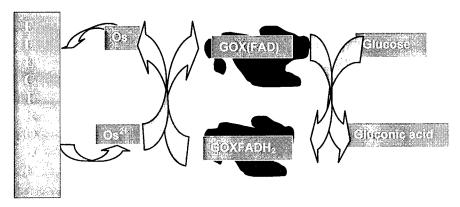


Figure 7 schematic diagram showing the reactions occurring in the hydrogel.

Similar sensors were fabricated and evaluated using chronoamperometry technique. The voltage set at 0.4V vs Ag/AgCl where all Os<sup>+</sup> in redox polymer has already been converted to Os<sup>2+</sup>. Without any glucose a constant current was obtained all through the length of the experiment for all the electrodes in the array. Figure 8 shows a chronoamperometry data obtained with successive addition of glucose versus the glucose concentration. With each successive glucose addition a corresponding increase in current was obtained resulting in a staircase type of data. A plot of current increase (steps) versus the concentration of glucose yielded a straight line (figure 9). These results are not accompanied by proper mixing as one would expect in a flowing system as in vivo where blood sugar is uniform. Similar measurements in a flow cell to mimic a sensor in contact with blood are desirable. This will provide us with information about long term stability of this sensor. These sensors show good response to glucose a very important first step.

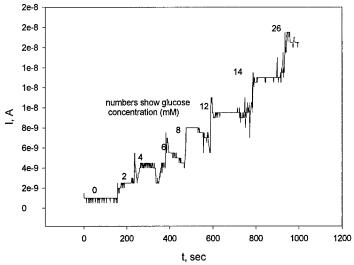


Figure 8. Amperometric responses of enzyme film to successive additions of glucose

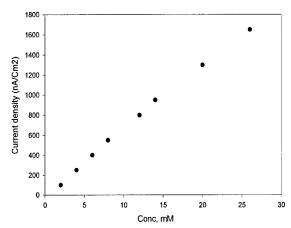


Figure 9. Step current versus glucose concentration on one element of microarray electrodes in amperometric detection

### **Conclusions**

We have fabricated micro-array gold electrodes on flexible mylar and polyimide sheets. After establishing the optimum fabrication conditions for reproducibility, we have produced a glucose redundant sensor array. Using conventional silicon microsensor fabrication methods, we have initially formed a five element array of microelectrodes consisting of Au microdisks. We were able to crosslink glucose oxidase enzyme with redox polymer using PEG-DA hydrogel. These micro-array sensors were individually addressable and were without discontinuities. There was no cross-talk between adjacent members. When Joined together the microarray electrodes behaved like one large electrode with peak current equivalent of sum of individual elements of array. This will be important when diagnosing any array element failure. Glucose oxidase enzyme exchanged electrons with redox polymer in the hydrogel catalyzing the oxidation of glucose by the enzyme. This reaction occurred in presence of oxygen- a very significant result since when it comes to implantation measurements will be made in presence of oxygen. For this redundant sensor array, we are next particularly interested in accuracy, precision, and its reliability. Our goal is to ensure that the enzyme and the redox polymer will remain intact to ensure the signal remain constant and be able to identify a failed element in the array.

#### Personnel

Michael V. Pishko, Professor, Department of Chemical Engineering, Penn State University Amos Mugweru, Postdoctoral Associate Becky Clark, Graduate Student

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# **Appendices**

Acronyms

CV: Cyclic voltammetry

bpy: bis-bipyridine

PEG-DA: poly(ethylene glycol) diacrylate

PVP-Os: poly[vinylpyridine Os(bis-bipyridine)<sub>2</sub>Cl]

# **Key Personnel Curriculum Vitae**

## **CURRICULUM VITAE**

Name: Michael V. Pishko, Ph.D.

Professor of Chemical Engineering Associate Professor of Chemistry

Associate Professor of Materials Science and Engineering

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### Education

Ph.D. - August 1992

Chemical Engineering (Dissertation topic: Implantable amperometric biosensors)

Supervisor: Prof. Adam Heller

University of Texas at Austin, Austin, TX 76712

Master of Science - December 1987

Chemical Engineering (Thesis topic: Conducting polymers)

Supervisor: Prof. Thomas Marrero

University of Missouri - Columbia, Columbia, MO 65211

Bachelor of Science - May 1986

Chemical Engineering (graduated Honors Scholar)

University of Missouri - Columbia, Columbia, MO 65211

#### **Experience**

Professor of Chemical Engineering (July 2005 to present)

The Pennsylvania State University, University Park, PA

Associate Professor of Chemistry (December 2003 to present)

Appointment by courtesy, The Pennsylvania State University, University Park, PA

Associate Professor of Materials Science and Engineering (July 2002 to present)

Appointment by courtesy, The Pennsylvania State University, University Park, PA

Associate Professor of Chemical Engineering (August 2001 to June 2005)

The Pennsylvania State University, University Park, PA

Assistant Professor of Chemical Engineering (January 1997 – July 2001)

Texas A&M University, College Station, TX 77843-3122

Research Scientist and Scientific Co-Founder (March 1996 – December 1996)

Sontra Medical, Inc., Cambridge, MA

Postdoctoral Associate (January 1995 – December 1996)

Supervisor: Prof. Robert Langer

Department of Chemical Engineering, Massachusetts Institute of Technology

Research Engineer (1992 - 1994)

E. Heller & Company (now Therasense, Inc. of Alameda, CA)

Graduate Research Assistant (August 1988 – August 1992)

Supervisor: Prof. Adam Heller

Department of Chemical Engineering, University of Texas at Austin

Graduate Research Assistant (June 1986 – December 1987)

Department of Chemical Engineering, University of Missouri - Columbia

Summer Research Intern (May 1985 – August 1985)

Argonne National Laboratory, Argonne, IL

#### Honors and Awards

Associate Editor, IEEE Sensors Journal, 2003-2005.

Guest Editor, IEEE Sensors Journal, Biosensors special issue, June 2003.

Editorial Board, Sensor Letters, 2004-2006.

Editorial Board, Applied Biochemistry & Biotechnology, 2003-2005.

Editorial Board, IEEE Sensors Journal, 2003-2005.

Mary Jane Kugel Award, Juvenile Diabetes Research Foundation International, 2002
Texas A&M University, College of Engineering, Select Young Faculty Fellow, 2000-2001
Outstanding Young Scientist, Houston Society for Engineering in Medicine & Biology, 2000
Texas A&M University, College of Engineering, Phillips Petroleum Company Faculty Fellow, 1999 - 2000

Alfred P. Sloan Research Fellow, 1999 - 2001

NSF CAREER Award, 1999 - 2003

Biomedical Engineering Society Young Investigator Travel Award, 1997

NASA Graduate Training Grant Fellow, 1986 and 1987

## **External Research Support/Grants**

- 1. USARO STTR Phase II (sub contract from Lynntech, Inc.): "Bioelectrochemical fuel cells" 9/22/04-9/21/06, \$225,000, PI.
- 2. USAMRMC W81XWH-04-1-0780: "Microfabricated multianalyte sensor arrays for metabolite monitoring" 8/15/04-8/14/07, \$281,003, PI.
- 3. NSF BES-0426170: "SST: Ricin quantification in aqueous media" 8/1/04-7/31/07, \$300,000, co-PI.
- 4. NASA BIOTECH-01-0023-0131: "Microfabricated Optical Biosensor Arrays for In Situ Bioreactor Monitoring" 12/1/03-11/30/06, \$424,000, PI.
- 5. CIBA Vision, Inc.: "Sensors for Glucose Based on Fluorescence" 12/1/02 to 11/30/03, \$78,082, PI.
- 6. National Institutes of Health 5R01EB000684-02: "Vibrating Nanostructures for the Prevention of Biofouling on Implanted Devices" 10/1/02 to 9/30/05, \$929,775, PI.

- 7. National Science Foundation, BES-0210298 "NIRT: Nanoengineered shells for encapsulation and controlled release" 9/1/2002-8/31/2006, \$210,000, co-PI.
- 8. National Medical Technology Testbed, Inc.- USAMMC: "Electrochemical Microsensor Arrays" 10/1/00-9/30/2001, \$142,283, Principal Investigator.
- 9. NASA NAG 9-1372: "Microfabricated Optical Biosensor Arrays for Air Quality Monitoring" 10/1/00 9/30/04, \$289,461, Principal Investigator.
- 10. Juvenile Diabetes Foundation International subcontract from the University of Maryland, Baltimore County: "Implantable Glucose Sensors Based on a Fluorescence Lifetime Competitive Binding System" 10/1/00 9/31/01, \$50,180, co-Investigator.
- 11. Sontra Medical, Inc.: "Development of Patch-Type Glucose Sensor" 6/1/00 5/30/01, \$81,091, Principal Investigator.
- 12. National Science Foundation, ECS-991290: "Acquisition of a Multi-Purpose, Multi-User Mask Aligner" \$78,390, co-PI.
- 13. Henley Healthcare, Inc.: "Gels for the Delivery of Drugs" 2/1/00 1/31/01, \$47,800, Principal Investigator.
- 14. Texas Higher Education Coordinating Board, Advanced Research Program: "Implantable Microparticles for Intracellular and Extracellular Glucose Sensing" 1/1/2000 12/31/2001, \$171,746, Principal Investigator.
- 15. Texas Higher Education Coordinating Board, Advanced Technology Program: "Rapid Screening of Libraries of Genetically Engineered Cells Using Micropatterned Biomaterials" 1/1/2000 12/31/2001, \$68,753, Principal Investigator.
- 16. National Science Foundation, BES-9908439: "Development of an Implantable Optical Glucose Sensor" 9/1/99-8/31/2003, \$372,045, co-PI.
- 17. National Medical Technology Testbed, Inc.- USAMMC: "Electrochemical Microsensor Arrays" 4/1/99-3/31/2000, \$60,000, Principal Investigator.
- 18. Alfred P. Sloan Research Fellowship: 1999-2001, \$35,000, Principal Investigator.
- 19. National Science Foundation CAREER Award, CTS-9875372, 0196525: "Microfabrication of Highly Ordered Biosensor Arrays" 5/1/99-4/30/2004, \$225,000, Principal Investigator.
- 20. NASA: "Investigation of Neuronal Physiology in Simulated Microgravity using Smart Fluorescent Microcarriers and Bulk Near-infrared Sensors" 3/1/99 12/31/2003, \$572,126, co-PI.
- 21. Whitaker Foundation: "Optical Spectroscopy for Body Chemical Measurements" 12/1/98-11/31/99, \$70,000, co-investigator.
- 22. Whitaker Foundation: "Microfabrication of Implantable Biosensor Arrays" 9/1/98 8/31/2001, \$187,618, Principal Investigator.
- 23. Juvenile Diabetes Foundation International: "Noninvasive Glucose Sensing Using Reverse Sonophoresis in Combination with a Glucose Sensor Array" 8/1/98 7/31/2000, \$144,820, Principal Investigator.
- 24. Texas Higher Education Coordinating Board, Advanced Research Program: "Influence of Topography on Neovascularization of Biomaterials for Tissue Engineering" 1/1/98 8/31/2000, \$118,380, Principal Investigator.
- 25. NSF SBIR, DMI-9362052: "Remediation of Organic Pollution via Catalyzed Photooxidation of Pollutants in Air and on Surfaces" 3/1/94 12/31/97, \$64,352, Principal Investigator.

### **Refereed Journal Publications**

- 1. Zguris, J.; Pishko, M. "Nitric Oxide Sensitive Fluorescent Poly(ethylene) glycol Hydrogel Microstructures" submitted.
- 2. Allcock, H.; Phelps, M.; Barrett, E.; Pishko, M.; Koh, W. "Photolithographic Development of Polyphosphazene Hydrogels for Potential use in Microarray Biosensors" submitted.
- 3. Ainslie, K.; Sharma, G.; Dyer, M.; Grimes, C.; Pishko, M. "Attenuation of Protein Adsorption on Static and Oscillating Magnetostrictive Nanowires" *Nano Letters* accepted for publication.

- 4. Ibey, B.; Beier, H; Rounds, R.; Yadavalli, V.; Pishko, M.; Coté, G. "Competitive binding assay for glucose based on glycodendrimer-fluorophore conjugates" *Anal. Chem.* accepted for publication.
- 5. Lee, S.; Nayak, V.; Dodds, J.; Pishko, M.; Smith, N. "Glucose measurements with sensors and ultrasound" *Ultrasound Med. Biol.* **2005**, *31*(7), 971-7.
- 6. Zguris, J.; Itle, L.; Hayes, D.; Pishko, M. "Microreactor Microfluidic Systems with Human Microsomes and Hepatocytes for use in Metabolite Studies" *Biomedical Microdevices* **2005**, 7(2), 117-25.
- 7. Itle, L.; Pishko, M. "Cryopreservation of cell-containing poly(ethylene) glycol hydrogel microarrays" *Biotechnology Progress* **2005**, *21*(**3**), 1004-1007.
- 8. Stine, R.; Schengrund, C.; Pishko, M. "Comparison of Glycosphingolipids and Antibodies as Receptor Molecules for Ricin Detection" *Anal. Chem.* **2005**, *77*(9), 2882-8.
- 9. Zguris, J.; Itle, L.; Koh, W.-G.; Pishko, M. "A Novel Single-Step Fabrication of Heterogeneous Poly (ethylene) glycol Hydrogel Microstructures Containing Multiple Phenotypes of Mammalian Cells" *Langmuir* 2005, 21(9), 4168-74.
- 10. Itle, L.; Koh, W.; Pishko, M. "Hepatocyte Viability and Protein Expression within Surface Immobilized Hydrogel Microstructures" *Biotechnology Progress* **2005**, *21*(3), 926-32.
- 11. Koh, Won-Gun; Pishko, M. "Immobilization of multi-enzyme microreactors inside microfluidic devices" Sensors & Actuators B 2005, 106(1), 335-342.
- 12. Yadavalli, V.; Russell, R.; McShane, M.; Cote', G.; Pishko, M. "A Monte Carlo Simulation of Photon Propagation in Fluorescent Poly(ethylene glycol) Hydrogel Microsensors" *Sensors & Actuators B* **2005**, *105*, 365-377.
- 13. Zahr, A.; de Villiers, M.; Pishko, M. "Encapsulation of Drug Nanoparticles in Self-Assembled Macromolecular Nanoshells" *Langmuir* **2005**, *21*, 403-410.
- 14. Meiring, J.; Schmid, M.; Grayson, S.; Rathsack, B.; Johnson, D.; Kirby, R.; Kannappan, R.; Manthiram, K.; Hsia, B.; Hogan, Z.; Ellington, A.; Pishko, M.; Willson, C. "Hydrogel Biosensor Array Platform Indexed by Shape" *Chem. Mater.* **2004**, *16*, 5574-5580.
- 15. O'Neal, D. B.; Meledeo, M. A.; Davis, J.; Ibey, B.; Pishko, M.; Coté, G. "Oxygen sensor based on the fluorescence quenching of a ruthenium complex immobilized in a biocompatible poly(ethylene glycol) hydrogel" *IEEE Sensors Journal* **2004**, *4*(**6**), 728-734.
- 16. Hile, D.; Pishko, M. "Solvent-Free Protein Encapsulation within Biodegradable Polymer Foams" *Drug Delivery* **2004**, *11*, 287-293.
- 17. Stine, R.; Schengrund, C.; Pishko, M. "Heat-Stabilized Glycosphingolipid Films for Biosensing Applications" *Langmuir* **2004**, *20*, 6501-6506.
- 18. Mor, G.; Carvalho, M.; Varghese, O.; Paulose, M.; Pishko, M.; Grimes, C. "A Room Temperature TiO<sub>2</sub>-Nanotube Hydrogen Sensor Able to Photoactively Self-clean from Environmental Contamination" *J. Mater. Res.* **2004**, *19*(**2**), 628-634.
- 19. Yadavalli, V.; Pishko, M. "Biosensing in microfluidic channels using fluorescence polarization" *Anal. Chim. Acta.* **2004**, *507*(1), 123-128.
- 20. Yadavalli, V.; Koh, W.-G.; Lazur, G.; Pishko, M. "Microfabricated protein-containing poly(ethylene glycol) hydrogel arrays for biosensing" *Sensors & Actuators B: Chemical* **2004**, 97(2-3), 290-297.
- 21. Koh, W.-G.; Pishko, M. "Photoreaction injection molding of biomaterial microstructures" *Langmuir* **2003**, *19*(**24**), 10310-10316.
- 22. Koh, W.; Itle, L.; Pishko, M. "Molding of hydrogel microstructures to create multi-phenotype cell microarrays" *Anal. Chem.* **2003**, *75*, 5783-5789.
- 23. Koh, W.-G.; Revzin, A.; Simonian, A.; Reeves, T.; Pishko, M. "Control of Mammalian Cell and Bacteria Adhesion on Substrates Micropatterned with Poly(ethylene glycol) Hydrogels" *Biomedical Microdevices* **2003**, *5*(1), 11-19.
- 24. Gong, D.; Yadavalli, V.; Paulose, M.; Pishko, M.; Grimes, C. "Drug Release Characteristics of Nanoporous Alumina Capsules" *Biomedical Microdevices* **2003**, *5*(1), 75-80.

- 25. Grimes, C.; Ong, K.; Varghese, O.; Yang, X.; Mor, G.; Paulose, M.; Dickey, E.; Ruan, C.; Pishko, M.; Kendig, J.; Mason, A. "A Sentinel Sensor Network for Hydrogen Sensing" *Sensors* **2003**, *3*, 69-82.
- 26. Simonian, A.; Revzin, A.; Wild, J.; Elkind, J.; Pishko, M. "Characterization of Oxidoreductase/ Redox Polymer Electrostatic Film Assembly on Gold by Surface Plasmon Resonance Spectroscopy and FTIR" *Analytical Chimica Acta* **2002**, *446*, 201-212.
- 27. Koh, W.; Revzin, A.; Pishko, M. "Poly(ethylene glycol) Hydrogel Microstructures Encapsulating Living Cells" *Langmuir* **2002**, *18*, 2459-2462.
- 28. Pishko, M.; Revzin, A.; Simonian, A. "Mass Transfer in Amperometric Biosensors Based on Nanocomposite Thin Films of Redox Polymers and Oxidoreductases (invited)" *Sensors* **2002**, 2, 79-90.
- 29. Revzin, A.; Sirkar, K.; Pishko, M. "Glucose, Lactate, and Pyruvate Biosensor Arrays Based on Redox Polymer/Oxidoreductase Nanocomposite Thin Films Deposited on Photolithographically Patterned Gold Electrodes" Sensors & Actuators B 2002, 81, 359-368.
- 30. Revzin, A.; Russell, R.; Yadavalli, V.; Koh, W.; Deister, C.; Hile, D.; Mellott, M.; Pishko, M. "Fabrication of Poly(ethylene glycol) Hydrogel Microstructures Using Photolithography" *Langmuir* **2001**, *17*, 5440-5447.
- 31. Amirpour, M.; Lackowski, W.; Ghosh, P.; Crooks, R.; Pishko, M. "Growth of Mammalian Cells on Micropatterned Surfaces of Weak-Acid, Polyelectrolyte Hyperbranched Thin Films on Gold" *Analytical Chemistry* **2001**, *73*, 1560-1566.
- 32. Mellott, M.; Searcy, K.; Pishko, M. "Release of Protein from Highly Cross-Linked Hydrogels of Poly(ethylene glycol) Diacrylate Fabricated by UV Polymerization" *Biomaterials* **2001**, *22*, 929-941.
- 33. Russell, R.; Axel, A.; Shields, K.; Pishko, M. "Mass Transfer in Rapidly Photopolymerized Poly(ethylene glycol) Hydrogels Used for Chemical Sensing" *Polymer* **2001**, *42*, 4893-4901.
- 34. Hile, D.; Pishko, M. "Emulsion Polymerization of D,L-Lactide and Glycolide in Supercritical Carbon Dioxide" *J. Polym. Sci. A* **2001**, *39*(4), 562-570.
- 35. McShane, M.; Russell, R.; Pishko, M.; Coté, G. "Glucose Monitoring Using Implanted Fluorescent Microspheres" *IEEE Engineering in Medicine and Biology* **2000**, *19*(6), 36-45.
- 36. Cantrell, J.; McArthur, M.; Pishko, M. "Transdermal Extraction of Interstitial Fluid Using Low Frequency Ultrasound Quantified Using <sup>3</sup>H<sub>2</sub>O as a Tracer Molecule" *J. Pharm. Sci.* **2000**, 89(9), 1170-1179.
- 37. Sirkar, K.; Revzin, A.; Pishko, M. "Glucose and Lactate Biosensors Based on Redox Polymer/Oxidoreductase Nanocomposite Thin Films" *Anal. Chem.* **2000**, 72(13), 2930-2936.
- 38. McShane, M.; Rastegar, S.; Pishko, M.; Coté, G. "Monte Carlo Modeling for Implantable Fluorescent Analyte Sensors" *IEEE Transactions in Biomedical Engineering* **2000**, *47*(**5**), 624-632.
- 39. Russell, R.; Sirkar, K.; Pishko, M. "Preparation of Nanocomposite Poly(allylamine)-Poly(ethylene glycol) Thin Films Using Michael Addition" *Langmuir* **2000**, *16*(8), 4052-4054.
- 40. Hile, D.; Amirpour, M. L.; Akgerman, A.; Pishko, M. "Controlled Delivery of Active Basic Fibroblast Growth Factor from Microporous Poly(D,L-lactide-co-glycolide) Foams Prepared in Supercritical Carbon Dioxide" *J. Controlled Release* **2000**, *66*, 177-185.
- 41. Kost, J.; Mitragotri, S.; Gabbay, R.; Pishko, M.; Langer, R. "Non-invasive Measurement of Glucose and Other Analytes" *Nature Medicine* **2000**, *6*(**3**), 347-350.
- 42. Russell, R.; Simonian, A.; Wild, J.; Pishko, M. "Poly(ethylene glycol) Hydrogel Encapsulated Fluorophore-Enzyme Conjugates for Direct Detection of Organophosphorus Neurotoxins" *Anal. Chem.* **1999** *71*(**21**), 4909-4912.
- 43. Hile, D.; Pishko, M. "Ring-Opening, Precipitation Polymerization of Poly(D,L-lactide-coglycolide) in Supercritical Carbon Dioxide" *Macromolecular Rapid Communications* **1999**, 20(10), 511-514.

- 44. Russell, R.; Gefrides, C.; McShane, M.; Coté, G.; Pishko, M. "A Fluorescence-Based Glucose Biosensor Based on Concanavalin A and Dextran Encapsulated in a Poly(ethylene glycol) Hydrogel" *Anal. Chem.* **1999**, *71*(**15**), 3126-3132.
- 45. Franchina, J.; Lackowski, W.; Dermody, D.; Crooks, R.; Bergbreiter, D.; Sirkar, K.; Russell, R.; Pishko, M. "Electrostatic Immobilization of Glucose Oxidase in a Weak-Acid, Polyelectrolyte Hyperbranched Thin Film on Gold: Fabrication, Characterization, and Enzymatic Activity" *Anal. Chem.* **1999**, *71*(**15**), 3133-3139.
- 46. Ghosh, P.; Amirpour, M. L.; Lackowski, W.; Pishko, M.; Crooks, R. "A Simple Lithographic Approach for Preparing Patterned, Micron-Scale Corrals for Controlling Cell Growth" *Angew. Chem., Int. Edition* **1999**, *38*(11), 1592-1595.
- 47. Sirkar, K.; Pishko, M. "Amperometric Biosensors Based on Oxidoreductases Immobilized in Photopolymerized Poly(ethylene glycol) Redox Hydrogels" *Anal. Chem.* **1998**, *70*, 2888-2894.
- 48. Schmidtke, D. W.; Pishko, M. V.; Quinn, C. P.; Heller, A. "Statistics for Critical Decision Making Based on Readings of Pairs of Implanted Sensors" *Anal. Chem.* 1996, 68(17), 2845.
- 49. Pishko, M. V. "Macromolecular Wiring of Oxidoreductases and Potential Interesting Applications" *Trends in Polymer Science* **1995**, *3*(**10**), 342.
- 50. Quinn, C. P.; Pishko, M. V.; Schmidtke, D. W.; Ishikawa, M.; Wagner, J. G.; Raskin, P.; Hubbell, J. A.; Heller, A. "Kinetics of Glucose Delivery to Subcutaneous Tissue in Rats: A Study Utilizing Amperometric Biosensors" *American Journal of Physiology* **1995**, 269(Endocrinol. Metab. **32**), E155.
- 51. Csöregi. E.; Quinn, C.; Lindquist, S.-E.; Schmidtke, D.; Pishko, M.; Ye, L.; Katakis, I.; Heller, A. "Design, Characterization, and One-Point *In Vivo* Calibration of a Subcutaneously Implanted Glucose Electrode" *Anal. Chem.* **1994**, *66*(**19**), 3131.
- 52. Linke, B.; Kerner, W.; Kiwit, M.; Pishko, M.; Heller, A. "Amperometric Biosensor for *In Vivo* Glucose Sensing Based on Glucose Oxidase Immobilized in a Redox Hydrogel" *Biosensors and Bioelectronics* **1994**, *9*, 151.
- 53. Pishko, M. V.; Michael, A. C.; Heller, A. "Amperometric Glucose Microelectrodes Prepared through Immobilization of Glucose Oxidase in Redox Hydrogels" *Anal. Chem.* **1991**, *63* (20), 2268.
- 54. Pishko, M. V.; Katakis, I.; Lindquist, S.-E.; Heller, A.; Degani, Y. "Electrical Communication Between Graphite Electrodes and Glucose Oxidase/Redox Polymer Complexes" *Mol. Cryst. Liq. Cryst.* 1990, 190, 221.
- 55. Pishko, M. V.; Katakis, I.; Lindquist, S.-E.; Ye, L.; Gregg, B. A.; Heller, A. "Direct Electrical Communication between Graphite Electrodes and Surface Adsorbed Glucose Oxidase/Redox Polymer Complexes" *Angewandte Chemie, International Ed.* 1990, 29 (1), 82.

# Review Articles, Book Chapters and Editorials

- 1. Coté, G.; Pishko, M. "Editorial: Special Issue on Biosensors" *IEEE Sensors Journal* **2003**, 3(3), 251-266.
- 2. Coté, G.; Lec, R.; Pishko, M. "Emerging Biomedical Sensing Technologies and Their Applications" *IEEE Sensors Journal* **2003**, *3*(3), 251-266.
- 3. Pishko, M. "Recent Advances in Biomaterials" in <u>Encyclopedia of Chemical Processing and Design, Vol. 69, Supplement 1</u> R. G. Anthony and J. J. McKetta, ed., Marcel Dekker, New York, 2002.
- 4. Pishko, M. "Analysis: Glucose Monitoring by Reverse Iontophoresis" *Diabetes Technology & Therapeutics*, **2000**, *2*(**2**), 207-208.
- 5. Pishko, M. "Biomaterials" *IEEE Engineering in Medicine and Biology* **1999**, *18*(1), 19-20.
- 6. Shastri, V.; Pishko, M. "Biomedical Applications of Electroactive Polymers" in <u>Electrical and Optical Polymer Systems: Fundamentals, Methods, and Applications, Wise, D., Wnek, G., Trantolo, D., Cooper, T., and J. Gresser, ed. Marcel Dekker, New York, 1998.</u>

- 7. Pishko, M. V. and Heller, A. (invited) "Enzyme Electrodes" in McGraw-Hill Yearbook of Science and Technology, 1994.
- 8. Kerner, W.; Lindquist, S.-E.; Pishko, M. V.; Heller, A. "Amperometric Glucose Sensor Containing Glucose Oxidase, Cross-Linked with Redox Gels" in *In Vivo* Chemical Sensors: Recent Developments, Alcock, S. J. and Turner, A. P. F., ed. Cranfield Press; Bedford, UK; 1993.

## **Issued Patents**

- 1. A. Heller, M. Pishko; "Subcutaneous Glucose Electrode" U.S. Patent 6,881,551.
- 2. A. Heller, M. Pishko; "Subcutaneous Glucose Electrode" U.S. Patent 6,514,718.
- 3. S. Rowe, J. Kost, S. Mitragotri, M. Pishko, M. Davis; "Ultrasound enhancement of transdermal transport" U.S. Patent 6.491,657.
- 4. G. Cote', M. Pishko, K. Sirkar, R. Russell, R. Anderson; "Compositions and Methods for Analyte Detection" U.S. Patent 6,485,703.
- 5. A. Heller, M. Pishko; "Subcutaneous Glucose Electrode" U.S. Patent 6,329,161.
- 6. A. Heller, M. Pishko; "Subcutaneous Glucose Electrode" U.S. Patent 6,284,478.
- 7. S. Rowe, J. Kost, S. Mitragotri, M. Pishko, M. Davis; "Ultrasound Enhancement of Transdermal Transport" U.S. Patent 6,234,990.
- 8. A. Heller, M. Pishko; "Subcutaneous Glucose Electrode" U.S. Patent 6,162,611.
- 9. A. Heller, M. Pishko; "Electrochemical Measurement System" U.S. Patent 6,121,009.
- 10. A. Heller, M. Pishko, E. Heller; "Photocatalyst-Binder Compositions" U.S. Patent 6,093,676.
- 11. A. Heller, M. Pishko; "Electrochemical Measurement System" U.S. Patent 6,083,710.
- 12. A. Heller, M. Pishko; "Subcutaneous Glucose Electrodes" U.S. Patent 5,965,380.
- 13. M. Johnson, S. Mitragotri, D. Blankschtein, R. Langer, M. Pishko, J. Kost; "Chemical and Physical Enhancers and Ultrasound for Transdermal Drug Delivery" U.S. Patent 5,947,921.
- 14. A. Heller, M. Pishko, E. Heller; "Photocatalyst-Binder Compositions" U.S. Patent 5,854,169.
- 15. A. Heller, M. Pishko, E. Heller; "Photocatalyst-Binder Compositions" U.S. Patent 5,849,200.
- 16. A. Heller, M. Pishko, E. Heller; "Photocatalyst-Binder Compositions" U.S. Patent 5,616,532.
- 17. A. Heller, M. Pishko; "Subcutaneous Glucose Electrodes" U.S. Patent 5,593,852.
- 18. B. Gregg, A. Heller, W. Kerner, M. V Pishko, I. Katakis; "Enzyme Electrodes" U.S. Patent 5,264,105.
- 19. B. Gregg, A. Heller, W. Kerner, M. Pishko, I. Katakis; "Enzyme Electrodes" U.S. Patent 5,264,104.

# **Conference Proceedings**

- 1. Itle, L.; Zguris, J.; Pishko, M. "Cell-based bioassays in microfluidic systems" *Proceedings-SPIE* **2004**, *5588*, 9-18, Smart Medical and Biomedical Sensor Technology II, Brian M. Cullum, Ed.
- 2. Stine, R.; Schengrund, M.; Pishko, M. "Stable, nanoscale glycosphingolipid films for use in sensing applications" *Materials Research Society Proceedings* **2004**, Vol. 823, W12.2.1.
- 3. Yadavalli, V.; Pishko, M. "Biosensing in microfluidic channels using fluorescence polarization" *Materials Research Society Proceedings* **2003**, Vol. 733, N7.11.
- 4. Pishko, M. "Cells in Micropatterned Hydrogels: Applications in Biosensing" in BioMEMS. <u>Fabrication and Applications of Analytical Devices</u>, 2<sup>nd</sup> Ed., Knowledge Press, Inc., Brookline, MA, 2003.
- 5. Elms, R.D.; Good, T.; Klaus, D.; Pishko, M. "Chemical and Gravity Dependent Factors affecting Escherchia coli Lag Phase Termination" *Gravitational and Space Biology Bulletin* **2002**, *16*(1), 21.
- 6. Koh, W.-G.; Pishko, M. "Cells in Micropatterned Hydrogels: Applications in Biosensing" *Materials Research Society Proceedings* **2002**, Vol. 723, O5.5.

- 7. O'Neal, D. P.; Meledeo, M. A.; Pishko, M.; Cote, G. "Feasibility of an on-line fluorescence-based optical sensor for oxygen monitoring in cell culture media" *Proceedings-SPIE* **2002**, 4624, 89-94, Optical Diagnostics and Sensing of Biological Fluids and Glucose and Cholesterol Monitoring II, Alexander V. Priezzhev; Gerard L. Cote; Eds.
- 8. Meledeo, M.; Ibey, B.; O'Neal, P.; Pishko, M.; Coté, G. "Investigation of pH and temperature effects on FRET systems for glucose sensing" *Proceedings-SPIE* **2002**, 4624, 55-65, <u>Optical Diagnostics and Sensing of Biological Fluids and Glucose and Cholesterol Monitoring II</u>, Alexander V. Priezzhev: Gerard L. Cote: Eds.
- 9. Koh, W.-G.; Pishko, M. "Chemical Sensor Arrays Using Biorecognition Molecules and Cells in Micropatterned Hydrogels" *Proceeding of the 32<sup>nd</sup> International Conference on Environmental Systems* **2002**, article 2002-01-2455.
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- 13. Mellott, M.; Revzin, A.; Hile, D.; Pishko, M. "Release of Proteins from Photopolymerized Poly(Ethylene Glycol) Hydrogels" *Proceedings of the International Symposium on the Controlled Release of Bioactive Materials* **2000**, 27, 8010.
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- 15. Russell, R.; Cote, G.; Pishko, M. "Optical Glucose Sensors Based on Photopolymerized Poly(ethylene glycol) Hydrogels" Digest of Papers of the 2000 World Congress on Medical Physics and Biomedical Engineering and the Proceedings of the 22<sup>nd</sup> Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2000, Paper TH-FXH-70.
- 16. Revzin, A.; Mellott, M.; Hile, D.; Pishko, M. "Controlled Released of Growth Factors from Micropatterned Hydrogels" *Transactions of the Sixth World Biomaterials Congress* 2000, Vol. 1, 232.
- 17. Ghosh, P.; Amirpour, M. L.; Lackowski, W.; Pishko, M.; Crooks, R. "A Simple Lithographic Approach for Preparing Patterned, Micron-Scale Corrals for Controlling Cell Growth" *Polymer Preprints* **1999**, 40(1), 423-424.
- 18. Russell, R.; Pishko, M.; Gefrides, C.; Cote, G. "A Fluorescent Glucose Assay using Poly-L-Lysine and Calcium Alginate Microencapsulated TRITC-Succinyl-Concanavalin A and FTIC-Dextran" *Proceedings of 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society* Oct 29 Nov 1, **1998**, Hong Kong, pg 2858 2861.
- 19. Sirkar, K. and Pishko, M. "Thin Film Amperometric Biosensors formed by Photopolymerization of PEG Copolymers" *Annals of Biomedical Engineering* **1998**, *26*(Supplement 1), S-37.
- 20. Mellott, M., Searcy, K. and Pishko, M. "Controlled Release of Proteins from Highly Crosslinked PEG Microspheres" *Annals of Biomedical Engineering* **1998**, *26*(Supplement 1), S-121.

- 21. Sirkar, K. and Pishko, M. "Photopolymerized Redox Hydrogel Biosensors" *Proceedings of the 25<sup>th</sup> International Symposium on Controlled Release of Bioactive Materials* **1998**, p. 116-117
- 22. Mellott, M., Searcy, K. and Pishko, M. "Transport Properties of PEG Gels" *Proceedings of the 25<sup>th</sup> International Symposium on Controlled Release of Bioactive Materials* **1998**, p. 900-901.
- 23. Sirkar, K. and Pishko, M. "Photopolymerized Redox Copolymers for Patterned Amperometric Biosensors" *Annals of Biomedical Engineering* **1997**, *25*(Supplement 1), S-1.
- 24. Heller, A.; Schwitzgebel, J.; Pishko, M.; Ekerdt, J. "Environmental Photoelectrochemistry" *Proceedings of the Electrochemical Society* **1994**, *94-19*, 1-9.

#### **Invited Presentations**

- 1. Purdue University, Department of Biomedical Engineering "Minimization of biofouling using vibrating nanowire arrays" West Lafayette, IN, March 2005.
- 2. 32<sup>nd</sup> ACS Northeast Regional Meeting, Session: Surface modification for coating and dispersion technology III "Magnetoelastic nanowire arrays for the prevention of biofouling" Rochester, NY, November 2004.
- 3. Optics East 2004, Session: Smart medical and biomedical sensor technology IV "Cell-based bioassays in microfluidic systems" Philadelphia, PA, October 2004.
- 4. Gordon Research Conference: Bioanalytical Sensors "Glucose Sensors Based on Fluorescence" Queen's College, Oxford, UK, July 2004.
- 5. Governor's Bionanotechnology Initiative Distinguished Speaker, "Oxidoreductase/Redox Polymer Thin Films for Amperometric Sensing" Louisiana Tech University, Ruston, LA, January 2004.
- 6. 2<sup>nd</sup> Annual Conference on Biodefense and Homeland Security, "Detecting and Characterizing Biological Agents with Biosensors" Milton Hershey Medical Center, Hershey, PA, May 2003.
- 7. Nanotech and Biotech Convergence 2003 "Microfabricated Cell-Based Biosensors and Biosensor Arrays" Stamford, CT, May 2003.
- 8. Pennsylvania State University, College of Medicine, Department of Biochemistry and Molecular Biology "Microdevices for Biosensing" Hershey, PA, December 2002.
- 9. CIBA Vision "Hydrogel-based sensors for glucose" Duluth, GA, October 2002.
- 10. Louisiana Tech University, Institute for Micromanufacturing "Microfabricated Cell-Based Biosensors and Biosensor Arrays" Ruston, LA, October 2002.
- 11. Nanotech and Biotech Convergence 2002 "Microfabricated Cell-Based Biosensors and Biosensor Arrays" Stamford, CT, May 2002.
- 12. BioMEMS 2002 "Cells in Micropatterned Hydrogels: Applications in Biosensing" Cambridge, MA, April 2002.
- 13. Argose, Inc. "Strategies for Measuring Glucose in Interstitial Fluid" Waltham, MA, June 2001.
- 14. Gordon Research Conference, Illicit Substance Detection: Biowarfare Agents "Cell and Tissue Based Biosensing" Mount Holyoke College, South Hadley, MA, June 2001.
- 15. 199<sup>th</sup> National Meeting of the Electrochemical Society, Bioelectroanalytical Chemistry Symposium "Amperometric Biosensors Based on Nanostructured Redox Polymer Thin Films" Washington, D.C., March 2001.
- 16. University of Houston "Microscale and Nanoscale Hydrogels for Chemical Sensing" Department of Chemical Engineering, Houston, TX, February 2001.
- 17. University of Pittsburgh "Microscale and Nanoscale Hydrogels for Chemical Sensing" Department of Chemical Engineering, Pittsburgh, PA, January 2001.
- 18. Guilford Pharmaceuticals, Inc. "Solvent-Free Encapsulation of Protein-Based Drugs in Biodegradable Polymers" Baltimore, MD, October 2000.

- 19. University of Maryland Baltimore County "Hydrogels for Chemical Sensing" Department of Biochemical Engineering, Baltimore, MD, October 2000.
- 20. Rice University "Hydrogels for Chemical Sensing" Departments of Bioengineering and Chemical Engineering, Houston, Texas, September 2000.
- 21. University of Southern California "Hydrogels for Chemical Sensing" Department of Chemical Engineering, Los Angeles, CA, September 2000.
- 22. Pennsylvania State University "Hydrogels for Chemical Sensing" Department of Chemical Engineering, State College, PA, September 2000.
- 23. University of Iowa "Hydrogels for Chemical Sensing" Center for Biocatalysis and Bioprocessing, Iowa City, Iowa, February 2000.
- 24. Abbott Laboratories, Inc. "Optical Glucose Sensors Based on Photopolymerized Poly(ethylene glycol) Hydrogels" Diagnostics Division, Abbott Park, IL, November 1999.
- 25. Abbott Laboratories, Inc. "Amperometric Biosensors Based on Photopolymerized Redox Hydrogels and Nanocomposite Thin Films" Diagnostics Division, Abbott Park, IL, November 1999.
- 26. Seventeenth Annual Houston Conference on Biomedical Engineering Research "Implantable and Minimally Invasive Systems for Glucose Sensing and Closed Loop Insulin Delivery" Houston, Texas, February 1999.
- 27. University of Texas at Austin "Hydrogels for Chemical Sensing" Department of Chemical Engineering, January 1999.
- 28. Dartmouth College "Redox Polymer/Oxidoreductase Complexes for Biosensor Applications" Bioengineering Program, Hanover, NH, December 1995.
- 29. Medisense Corporation "Biosensors Based on Redox Polymer/Oxidoreductase Complexes" Waltham, MA, September 1995.
- 30. University of Tokyo "Wired Enzyme Electrodes" Department of Chemistry, Tokyo, Japan, January 1992.
- 31. NASA Symposium Series: Life Support *In Situ* Sensors Technology Meeting "Electrical Wiring of Redox Enzymes" Jet Propulsion Laboratories, Pasadena, CA October 1991.

# **Oral and Poster Presentations**

- 1. Zguris, J.; Cote', G.; <u>Pishko, M.</u> "Microfabricated optical biosensor arrays for in situ bioreactor monitoring" Oral presentation, NASA Cell Science Conference, Galveston, TX, February 2005.
- 2. <u>Ainslie, K.</u>; Pishko, M. "Vibrating nanostructures for the prevention of biofouling" Oral presentation, American Institute of Chemical Engineers Annual Meeting, Austin, TX, November 2004.
- 3. Zahr, A.; Pishko, M. "Layer-by-layer assembly for the drug delivery of chemotherapeutics" Oral presentation, American Institute of Chemical Engineers Annual Meeting, Austin, TX, November 2004.
- 4. <u>Stine, R.</u>; Schengrund, C.; Pishko, M. "Heat stabilized ganglioside films for biotoxin sensing" Oral presentation, American Institute of Chemical Engineers Annual Meeting, Austin, TX, November 2004.
- 5. <u>Itle, L.</u>; Zguris, J.; Pishko, M. "Cell-based biosensors utilizing poly(ethylene glycol) hydrogel microstructures" Oral presentation, American Institute of Chemical Engineers Annual Meeting, Austin, TX, November 2004.
- 6. Zguris, J.; Pishko, M. "Microfabricated optical biosensors for in situ bioreactor monitoring" Oral presentation, American Institute of Chemical Engineers Annual Meeting, Austin, TX, November 2004.
- 7. <u>Ibey, B.</u>; Yadavalli, V.; Thomas, H.; Schengrund, C.; Pishko, M.; Cote', G. "Development of an implantable blood glucose monitor using a competitive binding fluorescent assay in

- poly(ethylene glycol) microspheres" Poster presentation, Fourth Annual Diabetes Technology Meeting, Philadelphia, PA, October 2004.
- 8. <u>Lee, S.</u>; Newnham, R.; Pishko, M.; Smith, N. "Noninvasive ultrasound glucose monitoring and insulin delivery using the low-profile cymbal array" Oral and poster presentations, Fourth Annual Diabetes Technology Meeting, Philadelphia, PA, October 2004.
- 9. <u>Itle, L.</u>; Koh, W.; Pishko, M. "Multi-phenotypic cell based biosensors" Poster presentation, American Chemical Society National Meeting, Philadelphia, PA, Aug. 2004.
- Zguris, J.; Pishko, M. "Microfabricated optical biosensors for in situ bioreactor monitoring" Poster presentation, American Chemical Society National Meeting, Philadelphia, PA, Aug. 2004.
- 11. <u>Dyer, M.</u>; Ainslie, K.; Sharma, G.; Grimes, C.; Pishko, M. "Protein adsorption on nanostructures" Poster presentation, American Chemical Society National Meeting, Philadelphia, PA, Aug. 2004.
- 12. Zahr, A.; Pishko, M. "Nanoencapsulation for drug delivery of chemotherapeutics" Poster presentation, American Chemical Society National Meeting, Philadelphia, PA, Aug. 2004.
- 13. <u>Stine, R.</u>; Schengrund, C.; Pishko, M. "Nanometer scale ganglioside thin films for biotoxin sensing" Poster presentation, American Chemical Society National Meeting, Philadelphia, PA, Aug. 2004.
- 14. <u>Kim, S.</u>; Kim, B.; Pishko, M. "Encapsulation of enzymes within polymer spheres to create novel optical micro- and nanosensors" Poster presentation, American Chemical Society National Meeting, Philadelphia, PA, Aug. 2004.
- 15. <u>Stine, R.</u>; Schengrund, C.; Pishko, M. "Stable, Nanoscale Glycosphingolipid Films for Use in Sensing Applications" Oral Presentation, 2004 Annual Meeting of the Institute for Biological Engineering, Fayetteville, AR, Jan. 2004.
- 16. <u>Yadavalli, V.</u>; Pishko, M. "Sensing in Microfluidic Devices Using Fluorescence Polarization" Oral presentation, 2003 Annual Meeting of the American Institute of Chemical Engineers, San Francisco, CA, November 2003.
- 17. <u>Koh, W.-G.</u>; Itle, L.; Pishko, M. "Photoreaction Injection Molding of Biomaterial Microstructures and Its Application to Create Multi-phenotype Cell Microarrays" Oral presentation, 2003 Annual Meeting of the American Institute of Chemical Engineers, San Francisco, CA, November 2003.
- 18. <u>Itle, L...</u>; Koh, W.-G.; Pishko, M. "Protein Production in Cell Containing Hydrogel Matrices for High Throughput Drug Screening" Oral presentation, 2003 Annual Meeting of the American Institute of Chemical Engineers, San Francisco, CA, November 2003.
- 19. Meiring, J.; Schmid, M.; Grayson, S.; Rathsack, B.; Johnson, D.; Kirby, R.; Kannappan, R.; Manthiram, K.; Stotts, J.; Hogan, Z.; Russell, R.; Pishko, M.; Ellington, A.; Willson, C. "Hydrogel biosensor arrays indexed through shape recognition" ACS Summer Meeting, 2003.
- 20. <u>Ibey, B.L.</u>; Coté, G. L.; Yadavalli, V.; Gant, V. A.; Newmyer, K.; Pishko, M. V. "Analysis of Longer Wavelength AlexaFluor Dyes for Use in a Minimally Invasive Glucose Sensor" in IEEE EMBS Meeting. 2003. Cancun, Mexico.
- 21. Yadavalli, V.; Pishko, M. "Biosensing using fluorescence polarization in microfluidic channels" Oral Presentation, 2003 Materials Research Society Spring Meeting, San Francisco, CA, April 2003.
- 22. <u>Pishko, M.</u>; Koh, W.; Yadavalli, V.; Zguris, J.; Itle, L. "Chemical Microsensor Arrays Using Biorecognition Molecules and Cells in Micropatterned Hydrogels" Oral Presentation, 2003 NASA Bioastronautics Investigators' Workshop, Galveston, TX, January 2003.
- 23. <u>Koh, W.-G.</u>; Yadavalli, V.; Pishko, M. "Fabrication of immobilized enzyme microreactors in microfluidic devices" Oral presentation, 2002 Annual Meeting of the American Institute of Chemical Engineers, Indianapolis, IN, November 2002.

- 24. <u>Koh, W.-G.</u>; Pishko, M. "Chemical and biological sensors based on living cells in PEG microstructures" Oral presentation, 2002 Annual Meeting of the American Institute of Chemical Engineers, Indianapolis, IN, November 2002.
- 25. <u>Yadavalli, V.</u>; Koh, W.-G.; Pishko, M. "Microfabricated protein-containing poly(ethylene glycol) hydrogel arrays for biosensing" Oral presentation, 2002 Annual Meeting of the American Institute of Chemical Engineers, Indianapolis, IN, November 2002.
- 26. Cote', G.; <u>Pishko, M.</u> "A potentially implantable fluorescent glucose sensor based on molecular recognition in poly(ethylene glycol) hydrogels" Poster presentation, Second Annual Meeting of the Diabetes Technology Society, Atlanta, GA, October 2002.
- 27. Koh, W.-G.; <u>Pishko, M.</u> "Chemical Sensor Arrays Using Biorecognition Molecules and Cells in Micropatterned Hydrogels" Oral presentation, 32<sup>nd</sup> International Conference on Environmental Systems, San Antonio, Texas, July 2002.
- 28. Koh, W.-G.; <u>Pishko, M.</u> "Microfabricated Cell-Based Biosensors and Biosensor Arrays" Poster Presentation, Sensors for Biological Research and Medicine, National Institutes of Health, Bethesda, Maryland, June 2002.
- 29. Revzin, A.; Simonian, A.; <u>Pishko, M.</u> "Amperometric Biosensors Based on Nanostructured Redox Polymer Thin Films" Oral presentation, 201<sup>st</sup> National Meeting of the Electrochemical Society, Philadelphia, PA, May 2002.
- 30. Koh, W.-G., Pishko, M. "Cells in Micropatterned Hydrogels: Applications in Biosensing" Oral presentation, Materials Research Society Spring Meeting, San Francisco, CA, April 2002.
- 31. <u>Koh, W.-G.</u>; Revzin, A.; Pishko, M. "Mammalian Cells Encapsulated in Poly(ethylene glycol) Hydrogel Microstructures for Use as Biosensors" Oral presentation, Annual Meeting of the American Institute of Chemical Engineers, Reno, Nevada, November 2001.
- 32. Revzin, A.; Simonian, A.; Pishko, M. "Amperometric Biosensors for Glucose, Lactate, and Pyruvate Based on Nanocomposite Redox Polymer/Oxidoreductase Thin Films" Oral presentation, Annual Meeting of the American Institute of Chemical Engineers, Reno, Nevada, November 2001.
- 33. Revzin, A.; Simonian, A.; Sirkar, K.; Pishko, M. "Redundant Amperometric Biosensors Based on Redox Polymer/Oxidoreductase Nanocomposite Thin Films Deposited on Photolithographically Patterned Gold Electrodes" Oral presentation, Nineteenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 2001.
- 34. <u>Koh, W.</u>; Revzin. A.; Pishko, M. "Fabrication of Poly(ethylene glycol) Hydrogel Microstructures Encapsulating Living Cells" Oral presentation, Nineteenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 2001.
- 35. <u>Pishko, M.</u> "Microfabricated Optical Biosensor Arrays for Air Quality Monitoring" Poster Presentation, Bioastronautics Investigators Workshop, 17-19 January 2001, Galveston, Texas.
- 36. <u>Hile, D.</u>; Pishko, M. "Emulsion Polymerization of Biodegradable Polymers in Supercritical Carbon Dioxide" Oral Presentation, American Institute of Chemical Engineers 2000 Fall Meeting, Los Angeles, CA.
- 37. <u>Russell, R.</u>; Yadavalli, V.; Cote, G.; Pishko, M. "A Potentially Implantable Fluorescent Glucose Sensor Based on Molecular Recognition in Poly(ethylene glycol) Hydrogels" Oral Presentation, American Institute of Chemical Engineers 2000 Fall Meeting, Los Angeles, CA.
- 38. Sirkar, K.; Revzin, A.; Pishko, M. "Fabrication of Biosensor Arrays Using Electrostatically Complexed Multilayers Deposited on Patterned Electrodes" Oral Presentation, American Institute of Chemical Engineers 2000 Fall Meeting, Los Angeles, CA.
- 39. Revzin, A.; Russell, R.; Koh, W.-G.; <u>Pishko, M.</u> "Microfabricated Poly(ethylene glycol) Arrays for Chemical Sensing" Oral Presentation, American Institute of Chemical Engineers 2000 Fall Meeting, Los Angeles, CA.
- 40. <u>Axel, A.</u>; Russell, R.; Pishko, M. "Polymer Hydrogel Swelling" Poster Presentation, American Institute of Chemical Engineers 2000 Fall Meeting, Los Angeles, CA.

- 41. <u>Padera, R.</u>; Pishko, M.; Langer, R. "Biomaterials-Induced Vascularization, Vascular Permeability Factor and Mass Transport" Oral Presentation, 2000 Annual Fall Meeting of the Biomedical Engineering Society, Seattle, WA, October 2000.
- 42. Mellott, M.; Revzin, A.; Hile, D.; Pishko, M. "Release of Proteins from Photopolymerized Poly(Ethylene Glycol) Hydrogels" Poster Presentation, International Symposium on the Controlled Release of Bioactive Materials, Paris, France, July 2000.
- 43. O'Neal, D.; Russell, R.; Rastegar, S.; Pishko, M.; Cote, G. "Analysis of Fluorescence Light Propagation Through Skin for Biosensing" Poster Presentation, World Congress on Medical Physics and Biomedical Engineering, Chicago, IL, July 2000.
- 44. Russell, R.; Cote, G.; <u>Pishko, M.</u> "Optical Glucose Sensors Based on Photopolymerized Poly(ethylene glycol) Hydrogels" Oral Presentation, World Congress on Medical Physics and Biomedical Engineering, Chicago, IL, July 2000.
- 45. Amirpour, M.; Ghosh, P.; Lackowski, W.; Crooks, R.; <u>Pishko, M.</u> "Growth of Mammalian Cells on Micropatterned, Hyperbranched Polymer Thin Films" Poster Presentation, Nanoscience and Nanotechnology: Shaping Biomedical Research, National Institutes of Health, Bethesda, Maryland, June 2000.
- 46. <u>Simonian, A.</u>; Flounders, A.; Schoeniger, J.; Rainina, E.; Pishko, M.; Wild. J. "Enzyme Biosensors for Direct Detection of Organophosphates" Oral Presentation, The Sixth World Congress on Biosensors, San Diego, CA, May 2000.
- 47. <u>Sirkar, K.</u>; Revzin, A.; Cantrell, J.; Pishko, M. "Fabrication of Biosensor Arrays using Photolithography and Micro-contact Printing" Oral Presentation, The 197<sup>th</sup> Meeting of the Electrochemical Society, Toronto, Canada, May 2000.
- 48. Revzin, A.; Mellott, M.; Hile, D.; Pishko, M. "Controlled Released of Growth Factors from Micropatterned Hydrogels" Oral Presentation, Sixth World Biomaterials Congress 2000, Kamuela, Hawaii, May 2000.
- 49. <u>Russell, R.</u>; Pishko, M.; McShane, M.; Cote, G.; Rastegar, S. "Monte Carlo Simulations of Photon Propagation in Poly(ethylene glycol) Hydrogel Based Fluorescent Biosensors" Poster Presentation, American Chemical Society National Meeting, San Francisco, CA, March 2000.
- 50. Russell, R.; Pishko, M.; Simonian, A.; Wild, J. "Poly(ethylene glycol) Hydrogel Encapsulated Fluorophore Enzyme Conjugates for Direct Detection of Organophosphorus Neurotoxins" Poster Presentation, American Chemical Society National Meeting, San Francisco, CA, March 2000.
- 51. <u>Crooks, R.</u>; Ghosh, P.; Lackowski, W.; Amirpour, M.; Pishko, M. "Simple Approach for Preparing Patterned, Micron-scale Corrals for Controlling Cell Growth" Oral Presentation, American Chemical Society National Meeting, San Francisco, CA, March 2000.
- 52. Revzin, A.; Sirkar, K.; Pishko, M. "Nanocomposite Amperometric Biosensors for Glucose and Lactate Detection" Oral Presentation, Eighteenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 2000.
- 53. Mellott, M.; Revzin, A.; Hile, D.; Pishko, M. "Controlled Release of Proteins from Highly Crosslinked Hydrogels Photopolymerized from Poly(ethylene glycol)" Oral Presentation, Eighteenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 2000.
- 54. <u>Cantrell, J.</u>; McArthur, M.; Pishko, M. "Transdermal Extraction of Interstitial Fluid Using Low Frequency Ultrasound" Oral Presentation, Eighteenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 2000.
- 55. <u>Pishko, M.</u>; Hile, D.; Akgerman, A. "Delivery of Growth Factors from Microporous PLGA Foams Prepared in Supercritical Carbon Dioxide" Oral/Poster Presentation, The 5<sup>th</sup> US-Japan Symposium on Drug Delivery Systems, December 1999, Maui, Hawaii.
- 56. <u>Pishko, M.</u>; Cantrell, J.; McArthur, M. "Transdermal Extraction of Interstitial Fluid Using Low Frequency Ultrasound" Poster Presentation, The 5<sup>th</sup> US-Japan Symposium on Drug Delivery Systems, December 1999, Maui, Hawaii.

- 57. Mellott, M.; Pishko, M. "Highly Crosslinked Polyethylene Glycol Hydrogels: Swelling, Hydration and Release Characteristics" Oral Presentation, American Institute of Chemical Engineers 1999 Fall Meeting, Dallas, TX.
- 58. <u>Hile, D.</u>; Pishko, M. "Synthesis of Biodegradable Copolymers of Lactide and Glycolide in Supercritical Carbon Dioxide" Oral Presentation, American Institute of Chemical Engineers 1999 Fall Meeting, Dallas, TX.
- 59. <u>Hile, D.</u>; Amirpour, M.; Akgerman, A.; Pishko, M. "Delivery of Active Basic Fibroblast Growth Factor from Microporous Poly(D,L-lactide-co-glycolide) Foams Prepared in Supercritical Carbon Dioxide" Oral Presentation, American Institute of Chemical Engineers 1999 Fall Meeting, Dallas, TX.
- 60. Amirpour, M.; Crooks, R.; Ghosh, P.; Lackowski, W.; <u>Pishko, M.</u> "Growth and Dosing of Cells on Micropatterned Surfaces" Oral Presentation, American Institute of Chemical Engineers 1999 Fall Meeting, Dallas, TX.
- 61. Amirpour, M.; Crooks, R.; Ghosh, P.; Lackowski, W.; Pishko, M. "A Simple Lithographic Approach for Preparing Patterned, Micron-Scale Corrals for Controlling Cell Growth: Applications to Biosensing" Oral Presentation, Materials Research Society Fall Meeting, Boston, MA, December 1999.
- 62. <u>Crooks, R.</u>; Ghosh, P.; Lackowski, W.; Amirpour, M.; Pishko, M. "A Simple Lithographic Approach for Preparing Patterned, Micron-Scale Corrals for Biosensing" Oral Presentation, The Electrochemical Society Annual Meeting, Honolulu, HI, October 1999.
- 63. Ghosh, P.; Lackowski, W.; Amirpour, M.; Pishko, M.; Crooks, R. "Controlling Cell Growth on Plastic and Metal Surfaces Using Micro-contact Printing" Oral Presentation, American Chemical Society National Meeting, New Orleans, LA, August 1999.
- 64. <u>Lackowski, W.</u>; Ghosh, P.; Amirpour, M.; Pishko, M.; Crooks, R. "Spatially-Directed Cellular Adhesion on Micron-Scale Patterned Hyperbranched Poly(ethylene glycol)/Poly(acrylic acid) Films" Oral Presentation, American Chemical Society National Meeting, New Orleans, LA, August 1999.
- 65. Ghosh, P.; Amirpour, M.; Lackowski, W.; Pishko, M.; Crooks, R. "A Simple Lithographic Approach for Preparing Patterned, Micron-Scale Corrals for Controlling Cell Growth" Oral Presentation, American Chemical Society National Meeting, Anaheim, CA, March 1999.
- 66. <u>Russell, R.</u>; Gefrides, C.; Coté, G.; Pishko, M. "A Fluorescence-Based Glucose Biosensor Based on TRITC-Concanavalin A and FITC-Dextran Encapsulated in a Poly(ethylene glycol) Hydrogel" Seventeenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 1999.
- 67. Amirpour, M.; Ghosh, P.; Lackowski, W.; Crooks, R.; Pishko, M. "Controlled Growth of Cells on Micropatterned Surfaces" Seventeenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 1999.
- 68. <u>Hile, D.</u>; Amirpour, M.; Akgerman, A.; Pishko, M. "Controlled Delivery of Active Basic Fibroblast Growth Factor from Microporous Poly(D,L-lactide-co-glycolide) Foams Prepared in Supercritical Carbon Dioxide" Seventeenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 1999.
- 69. Peez, R., Dermody, D., Franchina, J., Jones, S., Bruening, M., Lackowski, W., Bergbreiter, D., Crooks, R., Sirkar, K., and Pishko, M. "Aqueous Solvation and Functionalization of Hyperbranched Polyelectrolyte Thin Films" Oral Presentation, Fall Meeting of the Materials Research Society, Boston, MA, December 1998.
- 70. Russell, R.; Pishko, M.; Gefrides, C.; Cote, G. "A Fluorescent Glucose Assay using Poly-L-Lysine and Calcium Alginate Microencapsulated TRITC-Succinyl-Concanavalin A and FTIC-Dextran" Oral Presentation, 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Hong Kong, Oct 29 Nov 1, 1998.

- 71. Sirkar, K. and <u>Pishko, M.</u> "Biosensors Based on Photopolymerized Poly(ethylene glycol) Hydrogels" Oral Presentation, 1998 Annual Meeting of the American Institute of Chemical Engineers, Miami, FL, November, 1998.
- 72. Mellott, M., and <u>Pishko, M.</u> "Controlled Release of Proteins from Highly Crosslinked PEG Microspheres" 1998 Annual Fall Meeting of the Biomedical Engineering Society, Cleveland, OH, October 1998.
- 73. Sirkar, K. and <u>Pishko, M.</u> "Thin Film Amperometric Biosensors formed by Photopolymerization of PEG Copolymers" 1998 Annual Fall Meeting of the Biomedical Engineering Society, Cleveland, OH, October 1998.
- 74. <u>Sirkar, K.</u> and Pishko, M. "Photopolymerized Redox Hydrogel Biosensors" Oral Presentation, 25<sup>th</sup> International Symposium on Controlled Release of Bioactive Materials, Las Vegas, NV, June 1998.
- 75. Mellott, M., Searcy, K. and Pishko, M. "Transport Properties of PEG Gels" Poster Presentation, 25<sup>th</sup> International Symposium on Controlled Release of Bioactive Materials, Las Vegas, NV, June 1998.
- 76. Mitragotri, S., Pishko, M., Kost, J., and Langer, R. "Ultrasound Mediated Transcutaneous Glucose Monitoring" Oral Presentation, Hot Topics in Neonatology, Washington, D.C., December 1997.
- 77. Sirkar, K. and <u>Pishko, M.</u>, "Photopolymerized Redox Copolymers for Lithographically Patterned Amperometric Biosensors" Poster Presentation, 5<sup>th</sup> North American Chemical Congress, Cancun, Mexico, November 1997.
- 78. Knorr, D. and <u>Pishko, M.</u>, "Electroenzymatic Fuel Cells" Oral Presentation, Electrochemical Society: South Texas Section Annual Fall Meeting, Round Top, TX, October 1997.
- 79. Sirkar, K. and <u>Pishko, M.</u>, "Photopolymerized Redox Copolymers for Patterned Amperometric Biosensors" Oral Presentation, Biomedical Engineering Society Annual Fall Meeting, San Diego, CA, October 1997.
- 80. Sirkar, K. and <u>Pishko, M.</u>, "Photopolymerizable Amperometric Wired Enzyme Electrodes" Poster Presentation, Gordon Conferences: Bioanalytical Sensors, Henniker, NH, July 1997.
- 81. <u>Pishko, M.</u>, Cook, J., Heller, E., Schwitzgebel, J., Gunawan, G., Ekerdt, J., and Heller, A., "Reduction of the Toxicity of Crude Oil on Water Through Sunlight Assisted Photocatalytic Oxidation on TiO<sub>2</sub> Coated Glass Microbubbles" Oral Presentation, American Chemical Society National Meeting, San Diego, CA, March 1994.
- 82. Heller, A., Gregg, B., <u>Pishko, M.</u>, "Amperometric Sensors Based on Electrically Wired Enzymes" Oral Presentation, American Chemical Society National Meeting, Washington, DC, April 1991.
- 83. <u>Pishko, M.</u>, Michael, A., Heller, A. "Glucose Microelectrodes Based on the Immobilization of Glucose Oxidase in 3-Dimensional Crosslinked Redox Polymer Networks" Oral Presentation, 3rd International Conference on Chemical Sensors; Cleveland, OH 1990.

#### **Professional Activities**

- Session Chair, Electrochemistry and Nanobiotechnology, Nanotechnology-Biotechnology Convergence 2003, Stamford, CT, May 2003
- Session Chair, Advances in Tissue Engineering, 2002 Annual Meeting of the American Institute of Chemical Engineers, Indianapolis, IN, November 2002.
- Session Chair, Biosensors, IEEE-EMBS 2002 Annual Meeting, Houston, TX, October 2002.
- Session Chair, Biosensors, Nanotechnology-Biotechnology Convergence 2002, Stamford, CT, May 2002
- Session Chair, Nanostructured Biomaterials, the Annual Meeting of the American Institute of Chemical Engineers, Reno, Nevada, November 2001.
- Session Chair, Biosensors, Nineteenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 2001.

Session Chair, Optical Glucose Sensing, World Congress on Medical Physics and Biomedical Engineering, Chicago, IL, July 2000.

Session Chair, Biochemical and Optical Sensors and Biosensors I, World Congress on Medical Physics and Biomedical Engineering, Chicago, IL, July 2000.

Session Chair, Biomaterials I, Eighteenth Annual Houston Conference on Biomedical Engineering Research, Houston, Texas, February 2000.

Chair, South Texas Section of the Electrochemical Society (6/00 - 7/01)

Vice-Chair, South Texas Section of the Electrochemical Society (7/99 – 6/00)

Secretary, South Texas Section of the Electrochemical Society (7/98 - 6/99)

Treasurer, South Texas Section of the Electrochemical Society (6/97 - 7/98)

Memberships: American Chemical Society, American Institute of Chemical Engineers, Materials Research Society, Biomedical Engineering Society

# **External Panels and Committees**

NIH/NCI Nanotechnology Panel, July 2005

NIH SBIR Panel, July 2005

NIH Chemistry/Biophysics NRSA Fellowship Panel, Chairperson, March 2005

NIH Chemistry/Biophysics NRSA Fellowship Panel, November 2004

NIH Chemistry/Biophysics NRSA Fellowship Panel, July 2004

NIH Surgery & Bioengineering Study Section, Ad hoc, February 2004

NIH Chemistry/Biophysics NRSA Fellowship Panel, November 2003

NIH Advanced Biomaterials Panel, August 2003.

Chair, AIBS-USAMRMC Technologies for Metabolic Monitoring Panel, July 2003.

NSF Sensors Panel, May 2003

NIH Chemistry/Biophysics NRSA Fellowship Panel, March 2003

NIH Chemistry/Biophysics NRSA Fellowship Panel, November 2002

NSF Bioengineering Review Panel, May 2001

NSF Sensing and Imaging Review Panel, December 2000

NSF SBIR Ultracapacitors Review Panel, August 2000

Juvenile Diabetes Foundation International Glucose Monitoring Review Panel, May 2000

Juvenile Diabetes Foundation International Medical Sciences Review Committee 1999-2002

Chair- Juvenile Diabetes Foundation International Glucose Monitoring Review Panel, Nov. 1999

NSF Biosystems on the Nanoscale Review Panel, November 1999

Juvenile Diabetes Foundation International Glucose Monitoring Review Panel, June 1999

NSF Science and Technology Center Site Review Committee, January 1999

### **Reviewer of Journals**

Analytical Chemistry

Angewandte Chemie

**Biomacromolecules** 

Biomaterials

Biotechnology Progress

Diabetes Technology and Therapeutics

Journal of the American Chemical Society

Journal of Controlled Release

Journal of Pharmaceutical Sciences

Journal of Physical Chemistry

Langmuir

Nature Biotechnology

Nature Materials

Proceedings of the National Academy of Sciences USA

# **Courses Taught**

- 1. Chemical Engineering Mass Transfer Operations
- 2. Chemical Engineering Thermodynamics II (Phase and reaction equilibria)
- 3. Materials Science in Medicine and Biology (Undergraduate/Graduate)
- 4. Polymer Engineering (Undergraduate/Graduate)
- 5. Biosensors (Graduate)
- 6. Nanotechnology-Biotechnology Convergence 2003 & 2004 Workshops (topics: cell-based bioassays, microfluidics, aptamers, piezoelectric sensors)

# Students Graduated and Researchers Supervised

# Masters of Science

- 1. Cheryl Rumbarger, M.S. "Development of polymeric nanoshells to encapsulate the hydrophilic chemotherapuetic drug, 5-fluorouracil, using a layer-by-layer assembly method" August 2005, presently at the Applied Research Laboratory, Penn State University.
- 2. Martin Gentile, M.S. "Escherichia coli adhesion to chemically modified poly(ethylene glycol) hydrogels" December 2004, presently at Pfizer, Inc.
- 3. Keith Newmyer, M.S. "The continued developed of an optical glucose sensor based on a FRET binding assay encapsulated within a poly(ethylene glycol) hydrogel" August 2004, presently at Bechtel-Bettis, Inc.
- 4. Rory Stine, M.S. "Utilizing thin polymer films to obtain highly specific protein adhesion on surfaces" June 2003, presently a Ph.D. student at the Pennsylvania State University.
- 5. Amy Urbanowicz, M.S. "The Development of a Rod-Coil Redox Polymer Composed of Biphenyl Esters and Poly(4-vinylpyridine)" June 2001, presently a high school teacher in Toledo, OH.
- 6. Jeffrey T. Cantrell, M.S. "The Determination of Glucose in Sonophoretically Extracted Interstitial Fluid and the Characterization of Ultrasound Parameters" July 2000, presently at Intel, Inc., Albuquerque, NM.
- 7. Kaushik Sirkar, M.S. "Amperometric Glucose Sensors Based on Photopolymerized Redox Hydrogels" December 1998, presently at Intel, Inc., Albuquerque, NM.

## Ph.D.

- 1. Jeanna Zguris, Ph.D. "Micro- and nanoscale devices for biosensing applications" August 2005, presently at Johnson & Johnson, Inc.
- 2. Laura Itle, Ph.D. "Creation of whole-cell based biosensors for high throughput drug screening and toxin detection" August 2005, presently at the Institute for Defense Analysis.
- 3. Rory Stine, Ph.D. "Lipid films for the production of biosensors and non-fouling surfaces" August 2005, presently at the Naval Research Laboratory.
- 4. Vamsi Yadavalli, Ph.D. "Toward the development of optical biosensing microsystems" March 2004, presently at the National Institutes of Health.
- 5. Won-Gun Koh, Ph.D. "Poly(ethylene) glycol hydrogel microstructures encapsulating living cells" February 2004, presently an Assistant Professor of Chemical Engineering at Yonsei University, Seoul, South Korea.
- 6. Alexander Revzin, Ph.D. "Development of Nanocomposite and Hydrogel Biosensors Based on Thin Film Technology" February 2002, presently at an Assistant Professor of Bioengineering at the University of California-Davis.
- 7. Michael B. Mellott, Ph.D. "Release of Biomolecules from Hydrogel Matrices of Photopolymerized Poly(ethylene glycol)" June 2001, presently at Intel, Inc., Portland, OR.
- 8. Ryan J. Russell, Ph.D. "Investigation of Poly(ethylene glycol) Hydrogel Networks for Optical Biosensing" December 2000, presently at Intel, Inc., Portland, OR.

- 9. David D. Hile, Ph.D. "Processing of Biodegradable Polymers in Supercritical and Liquid Carbon Dioxide" December 2000, presently at Cambridge Scientific, Cambridge, MA.
- 10. Kaushik Sirkar, Ph.D. "Amperometric Biosensor Arrays" September 2000, presently at presently at Intel, Inc., Albuquerque, NM.
- 11. Mary Lee Amirpour, Ph.D. "Topography of Biomaterials" December 1999, presently at Proctor & Gamble, Inc., Cincinnati, OH.

# Senior Researchers

- 1. Maureen Dyer, Ph.D., presently at Hanson Technologies, Carlisle, PA.
- 2. Aleksandr Simonian, Ph.D., presently an Associate Professor of Materials Science at Auburn University.
- 3. Bumsang Kim, Ph.D., presently an Assistant Professor of Chemical Engineering at Hongik University, Seoul, South Korea.

#### AMOS M. MUGWERU

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TEL. OFFICE: 814-863-7567 HOME: 814-861-3101

## **EDUCATION**

# Ph.D. Chemistry

# University of Connecticut, Storrs, CT, obtained Dec 2004

Thesis Title: "Voltammetric sensors for chemical toxicity and oxidative stress"

Major advisor: Dr. James F. Rusling

Master of Science in Chemistry

University of Nairobi, Kenya 1997.

Thesis title "Analytical applications of liquid junction potential"

Major advisor: Prof. M. Shamim

Bachelor of Science (1st Class honors)

J.K.U.A.T, Nairobi, Kenya, 1993

### **AWARDS AND HONORS**

- Electrochemical society (ECS) summer Fellowship (2004)
- Travel grant for 205<sup>th</sup> ECS meeting (2004)
- Japanese international cooperation Agency Award (JICA), (Paid all my tuition for MS studies for 2 yrs) 1994-1996

# RESEARCH EXPERIENCE

Postdoctoral Scholar- Jan 2005-Present,

Pennsylvania state university, University park, PA January 2005-present

Advisor: Dr. Michael Pishko

- Successively synthesized an osmium based polycationic redox polymer (POs-Ea) a molecule that is responsible for exchanging electrons with glucose oxidase enzyme.
- Used photolithography to fabricate patterned sensor arrays on flexible plastic substrates (mylar and polyimide).
- Successively crosslinked active glucose oxidase enzyme with redox polymer and biocompatible polyethylene glycol diacrylate hydrogel.
- Used amperometry and cyclic voltammetry to confirm activity of the enzyme and contribution of each sensor array element.
- The enzyme exchanged electrons with redox polymer both entrapped in a hydrogel network

Graduate Research Assistant: Department of Chemistry, University of Connecticut, Storrs, CT

Adviser: Dr. James F. Rusling,

8/02-12/04

- Developed in vitro toxicity sensors for DNA damage detection utilizing voltammetric techniques. Stable sensors for this purpose were constructed on electrodes using layer-by-layer electrostatic adsorption of DNA and bio-activating enzymes that mimic liver cytochrome P450s.
- Synthesized and characterized of Metallopolymer ruthenium and osmium complexes for catalytic oxidation.
- Investigated the enzyme-catalyzed activation pollutant products with GC-FID and GC-MS
- Characterized bio-reactive surfaces using Atomic Force Microscopy (AFM)
- Monitored the electrostatic layer-by-layer film growth using Quartz Crystal Microbalance (QCM) on gold resonators and UV/Vis on quartz slides
- Analyzed DNA adducts using PREP-LC and Capillary electrophoresis
- Fabricated sensors for DNA oxidative stress.
- Investigated inhibition of DNA damage by dietary antioxidants such as flavanoids,  $\alpha$ -tocopherol (vitamin E) and vitamin C using these fabricated sensors

#### **EMPLOYMENT HISTORY**

Jan 99- Dec 99 Teaching Assistant: Department of Chemistry, University of Connecticut, Storrs, CT

- Taught courses, Chem 128 and Chem 127 (include general and advanced chemistry)
- Conducted group discussions and facilitated laboratory sessions
- Graded exams, quizzes, and lab reports in addition to tutoring

Jan 00-Aug 02 Teaching assistant Department of Chemistry, University of Connecticut, Storrs, CT

- Taught courses Chem 232 and Chem 234 to seventh and eighth semester undergraduate students
- Courses focused on instrumental analysis, Quantitative Analysis, Instruments used include: GC, HPLC, UV-vis spectrophotometers, Atomic absorption spectrometer (AAS), Fluorescence Spectrometer, Infrared spectrometer and Potentiometers.
- Responsibilities included, Introducing the experiments and the various instruments operations, supervising students use the instruments and trouble shooting.
- Graded weekly reports and quizzes, Supervised exams and grading student presentations,
- Worked with the students on their different research projects.
- Helped redesign new experiments and helped students to come up with their own research projects

Nov. 97 – Jan 99 Jomo Kenyatta University of Agriculture and Technology (J.K.U.A.T.) Nairobi, Kenya

Chemistry instructor

- Taught general and advanced chemistry causes in undergraduates, general and advanced analytical chemistry courses.
  - Duties included, Teaching, setting examinations and marking them, coordinating discussion sections, and supervising laboratory sections.

#### **PUBLICATIONS**

- Mugweru, A.: Rusling, J. "Square wave Voltammetric Detection of Chemical DNA Damage with catalytic Poly(4-Vvinylpyridine)-Ru(bpy)<sub>2</sub><sup>2+</sup> films". *Anal. chem.* **2002**, 74, 4044-4049
- Mugweru A.; Rusling, J. "Catalytic square wave Voltammetric Detection of DNA with Reversible Metallopolymer-coated electrodes" *Electrochem. Commun.* **2001**, 3, 406-409
- Mugweru, A.; Jing Y.; Rusling, J. "Gomparison of Hemoglobin and Myoglobin for In Situ Metabolite Generation in Chemical Toxicity Sensors Using a Metallopolymer Catalyst for DNA Damage detection" *Electroanalysis*, 2004. 16, 1132-1138.
- Mugweru, A.; Bing, W.; Rusling, J. "Voltammetric Sensor for Oxidized DNA Using Ultrathin Films of Osmium and Ruthenium" Anal. Chem. 2004 76, 5557 – 5563
- Mugweru, A. "DNA Damage Inhibition by Dietary Antioxidants: Voltammetric detection of inhibition using Metallopolymer catalyst" Electrochemical society Interface Magazine, 2004, 13, 66
- Mugweru, A: "Rusling J. "Detection of inhibition of DNA damage by dietary antioxidants using sensors based on metallopolymer catalysts" Draft paper to electronalysis 2005.

# PROFESSIONAL TALKS

- Mugweru, A.,: Rusling J. "Electrochemical Toxicity sensors using layered polyion-DNA films".
   223<sup>rd</sup> ACS National meeting Orlando, Fl, United states, April 7-11, 2002
- Mugweru A. Rusling J. "Detection of DNA Damage Using Catalytic Square wave Voltammetry with Surface -Synthesized Metallo-polymer films" Book of Abstracts, 2003 Pittsburgh Conference, Orlando, FL, United States, March 9-14, 2003
- Mugweru, A.; Bing, W.; Rusling, J. "Biosensor for oxidized DNA using films containing [Os(bpy)<sub>2</sub>(PVP)<sub>10</sub>Cl]<sup>+</sup> and [Ru(bpy)<sub>2</sub>(PVP)<sub>10</sub>Cl]<sup>+</sup>" Book of Abstracts, 205<sup>th</sup> Electrochemical society Meeting, San Antonio, Texas United States, May 9-14, **2004.**
- Rusling, J.: Liping Z.; Jing, Y.: Mugweru, A.; Bingquan, W. "Electrochemical toxicity sensors based on toxic metabolite generation in layered protein-DNA films" FACSS Providence, RI, 2002
- Rusling, J.; Mugweru, A.; Liping Z.; Jing, Y. "Strategies for Voltammetric Toxicity Sensors Based on DNA Damage" International Society of Electrochemistry meeting in Germany 2001.
- Mugweru, A: Bing, W. Rusling, J. "Sensors for oxidized DNA using metallopolymer films" 228<sup>th</sup>
  ACS National meeting Philadelphia, PA, United states, August 22-26, 2004
- Mugweru, Amos,: Clark, B.L.; Pishko, M. V. "Electrochemical redundant micro-sensor arrays for glucose monitoring micro-fabricated on photopolymerized and micro-lithographically patterned polymer films" Scheduled for presentation at 230<sup>th</sup> ACS National meeting Washington, DC. USA, August 28-Sep 1 2005
- Clark, B.L.; Mugweru, A. Pishko, M. V. "Electrochemical glucose sensor for diabetes management" Scheduled for presentation at AICHE, Cincinnati, OH, USA 2005

# PROFESSIONAL ASSOCIATIONS

- American Chemical Society
- Electrochemical society

## **SKILLS**

## Research

- Educational training in analytical/ bioanalytical
- self-assembling multilayer membrane-like film,
- Nanofabrications, and bioelectrochemistry
- UV-Vis spectrometry
- Infrared spectrometry
- Gas chromatography
- High Performance Liquid Chromatography (HPLC)
- Inorganic synthesis
- lithography / Photolithography
- CMS-18 Thin Film Deposition Tool